

A. Double Patenting Rejection addressed

The Examiner has stated while both the instant application and co-pending U.S. Application Serial No. 10/021,533 are continuation-in-part applications of U.S. Application Serial No. 09/795,279 and both applications were filed as a result of the restriction requirement set forth in the parent application, the scope of the instant claims is different than the subject matter set forth in the '279 application. Therefore, the Examiner has advised that, if either one application is allowed, a terminal disclaimer should be filed. However, the Examiner did not indicate whether the Terminal Disclaimer should be filed with respect to Application Serial No. 09/795,279 or Serial No. 10/021,533. Clarification is respectfully requested. Furthermore, the filing of the Terminal Disclaimer will be deferred until allowable subject matter has been determined.

B. Section 112, first paragraph rejections addressed

Claims 1-9, 11-18, and 20-26 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, has possession of the claimed invention. The Office Action states that the limitation "0.2-30% by volume" recited in claims 1, 17 and 26 as currently pending is not supported by the originally filed specification or claims.

With respect to claims 1 and 21, these claims have been amended herein to replace the amount of alcohol from "0.2 - 30% by volume" to "0.2 - 13% by volume," thereby obviating this rejection. Support for this amendment can be found in the disclosure in paragraphs [0049] and [0051]. However, with respect to claim 26, it is respectfully pointed out that the rejected claim language "0.2 - 30% by volume" is not contained within claim 26. Withdrawal of this Section 112, first paragraph rejection is requested.

C. Section 112, second paragraph rejections addressed

Claims 1-25 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The Office Action states that the expression "sufficient amount of an acid to adjust the pH" in claims 1 and 21 renders the claims indefinite as to what amount of acid is encompassed by the claims. This rejection is respectfully traversed.

It is asserted that it is not necessary to recite the specific amount of acid required in each of the claimed compositions. Rather, all that is required is that a sufficient amount of the acid be added until the pH of the composition is between 2.45 and 4.6. It is well within the skill of persons skilled in the art to measure the pH of a solution (e.g., with a pH meter) during or after the addition of an acid to the solution and to make a determination as to whether the pH of the solution is between 2.45 and 4.6. It is asserted that pending claims 1-25 are clear and definite, and withdrawal of this rejection is requested.

D. Section 103(a) Rejections addressed

1. Claims 1-6 and 9-14, 16-23 and 25-26 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Yu et al. in view of Poli *et al.* and Wenniger. This rejection is respectfully traversed.

To establish a *prima facie* case of obviousness, it is well established that the prior art reference or combination of references must teach or suggest all the limitations of the claims. It is asserted that this burden has not been met by the Office Action and therefore a *prima facie* case of obviousness has not been established.

Claims 11 and 19 have been cancelled herein, and independent claims 1, 17 and 24 have been amended to further distinguish the claims over the cited art. More specifically, independent claim 1 has been amended to recite a method for the prophylaxis of lesions caused by a virus of the Herpesviridae or Poxviridae family, comprising topically applying to the lesion a composition **comprising** a synergistic combination, said synergistic combination consisting essentially of:

- 0.2-13% by volume of a C1-C3 alcohol or a C2-C4 diol and
- a sufficient amount of an acid to adjust the pH of the composition to between 2.45 and 4.6.

Independent claims 17 and 24 have been similarly amended. It is asserted that this amendment, which without question distinctly points out the novel, active component of the inventive composition, clearly distinguishes claim 1 over the cited art.

More specifically, the courts have ruled that when the phrase "consisting of" appears in a clause of the body of a claim rather than immediately following the preamble, it limits only that element set forth in that claim; the courts have declined to read this usage of "consisting of" as excluding all other elements from the claim as a whole. *Mannesmann*

Demag Corp. v. Engineered Metal Products Co., 793 R.2d 1279, 230 USPQ 45 (Fed. Cir. 1986). The term "comprising" implies that the **composition** can include other ingredients, such as fillers, etc. commonly used in formulating pharmaceutical compositions. Thus, the amendment to claim 1 clearly indicates that any element or ingredient other than 0.2-13.0% by volume of a C1-C3 alcohol or a C2-C4 diol and a sufficient amount of an acid to adjust the pH of the composition to between 2.45 and 4.6 is excluded from the effective synergistic combination of claim 1. However, the inventors are certainly entitled to include nonactive ingredients such as ointment, cream fillers, solvents, etc. in a formulation comprising this synergistic combination, and the transitional phrase "comprising" after the term "topical composition" allows for the addition of such ingredients. It would clearly undermine the entire patent process to allow a third party to make unimportant, insubstantial changes and substitutions to the synergistic combination of claim 1 in order to be able to circumvent the present invention by not allowing the language as provided in amended claim 1.

In contrast, Yu teaches a first example of composition containing two agents: an alpha hydroxyacid or alpha ketoacid and an amphoteric or pseudoamphoteric compound. The amphoteric or pseudoamphoteric compound is intentionally added to raise the pH of the composition in order to avoid skin irritation (see column 4, lines 2-12). Specifically, Yu states that a 1 molar aqueous solution of glycolic acid has a pH of 1.9, but the pH of the composition changes to 3.0 or 3.2 when an amphoteric compound such as arginine or creatinine, respectively, is combined with the glycolic acid solution. Thus, in this example Yu's active composition requires both an alpha hydroxyacid and an amphoteric compound. Therefore Yu's composition contains an element, i.e., an amphoteric compound, which is specifically excluded from the elements allowed in the synergistic combination of claim 1.

Yu also describes a formulation containing specific alpha hydroxy acids which are therapeutically effective for certain skin disorders without utilizing an amphoteric system (column 11, line 55-column 12, line 2), and provides glycolic acid as an example of an effective alpha hydroxy acid. However, as discussed above, the pH of a glycolic acid solution that does not include an amphoteric compound is **1.9**, which is outside of the pH range of 2.45 to 4.6 as required in claim 1. Accordingly, this alternative composition disclosed by Yu is also outside of the scope of amended claim 1.

Therefore, since Yu does not teach every element of the composition of claim 1, Yu cannot render claim 1 obvious. For the same reasons, Yu also does not teach every element

of claims 2-6 and 9-14, 16-23 and 25-26, and therefore claims 2-6 and 9-14, 16-23 and 25-26 are also nonobvious in light of Yu.

Next, the Office Action states that while Yu does not expressly teach that 1,3-butanediol is useful as a pharmaceutical vehicle, Wenniger teaches that 1,3-butanediol is useful as a solvent in numerous cosmetic marketed products. However, it is asserted that the Wenniger reference adds nothing to Yu that would render claims 1-6 and 9-14, 16-23 and 25-26 obvious. Even if there were a motivation to combine the references, the combination would not provide a method of treating an inflammation or lesion caused by a virus by contacting the inflammation or lesion with a composition **comprising** a synergistic combination, said synergistic combination consisting essentially of 0.2-13% by volume of a C1-C3 alcohol or a C2-C4 diol, and a sufficient amount of an acid to adjust the pH of the composition to between 2.45 and 4.6.

For the reasons presented above, the compositions of the present invention, considered as a whole as required by Section 103, would not have been *prima facie* obvious to one skilled in the art at the time this invention was made. None of the cited reference, alone or in combination, teach or suggest the compositions of claims 1-6 and 9-14, 16-23 and 25-26. Accordingly, withdrawal of the obviousness rejection of claims 1-6 and 9-14, 16-23 and 25-26 is respectfully requested.

2. Claims 1 and 7-8, 15, and 24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bhatia et al. in view of the article entitled "Disinfectant Drugs" and Remington. The Office Action states that while Bhatia et al. teach that 0.4 N hydrochloric acid is effective in inactivating sheep pox virus, they do not teach the use of hydrochloric acid with an alcohol, however the "Disinfectant Drugs" article teaches isopropanol at concentrations of 15% or above is effective as a single medicinal ingredient for disinfecting contact lenses, and Remington teaches that isopropanol and ethanol are very good pharmaceutical solvents. The Office Action then concludes one skilled in the art would have been obvious to combine the cited art because isopropanol is known to be useful as both a solvent and a disinfectant and hydrochloric acid is known to have virucidal activities against pox viruses.

The Office Action's position represents hindsight reconstruction or, at best, establishes it would have been "obvious to try." However, it is well established that "obvious to try" is not the standard in determining obviousness under Section 103(a). Without some suggestion

or incentive in the prior art references, independent of the hindsight provided by applicants' claims, it is improper to combine the prior art references in a manner necessary to show applicants' invention in a 35 U.S.C. § 103 obviousness rejection. *In re Samour*, 197 USPQ 1 (CCPA 1978); *In re Rinehart*, 189 USPQ 143 (CCPA 1976). Furthermore, "using an applicant's disclosure as a blueprint to reconstruct the claimed invention from isolated pieces of the prior art contravenes the statutory mandate of section 103 of judging obviousness at the point in time when the invention was made. *Grain Processing Corp v. American Maize- Prods. Co.* 840 F.2d 902, 907 5 USPQ2d 1788, 1792 (Fed. Cir. 1988).

It is asserted that the Examiner has only supplied references that appear to separately contain elements of the claimed invention without pointing to any motivation or suggestion in the references that they be combined. Furthermore, as discussed below, even if there were motivation to combine the cited references, the combination would not provide the method of the claimed invention.

First, Bhatia only discloses a method of combining goat-pox virus with hydrochloric acid and incubating this suspension for a period of time (see page 518, second column, last paragraph). In order to determine if the virus was still active after incubation with acid, Bhatia injected the suspension under the goats' skin and watched for signs of pain at the injection site. Thus, the Bhatia composition is actually a mixture of the goat-pox virus and a concentrated acid. However, Bhatia does not teach or even suggest combining the acid/goat pox mixture with an alcohol, let alone a method of for the prophylaxis of lesions in a mammal caused by a virus of the Herpesviridae or Poxviridae family by topically applying a composition **comprising** a synergistic combination, said synergistic combination consisting essentially of 0.2-13% by volume of a C1-C3 alcohol or a C2-C4 diol, and a sufficient amount of an acid to adjust the pH of the composition to between 2.45 and 4.6. Accordingly, there is no motivation to combine the teachings of Bhatia with the other cited references.

Next, even if there were motivation supplied in Bhatia to combine the teachings in the "Disinfectant Drugs" article (which there is not), the combination still would not provide the method of the claimed invention. As discussed above, the claims as amended herein are directed to a method of for the prophylaxis of lesions in a mammal caused by a virus of the Herpesviridae or Poxviridae family by topically applying a composition **comprising** a synergistic combination, said synergistic combination consisting essentially of 0.2-13% by volume of a C1-C3 alcohol or a C2-C4 diol, and a sufficient amount of an acid to adjust the pH of the composition to between 2.45 and 4.6. In contrast, the cited article only discloses

isopropanol at a concentration greater than or equal to 15%. Further, the article does not specifically teach that the isopropanol is inactivating viruses. Accordingly, it is asserted that the combination of Bhatia and the cited article would not provide the method of the claimed invention.

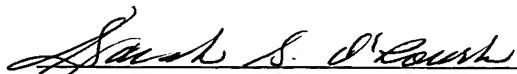
Finally, Remington only teaches that ethanol and isopropanol are useful pharmaceutical solvents. However, as stated in the 6th paragraph, 1st column on page 219 of Remington, isopropanol has an advantage over ethanol in that isopropanol contains "not over 1% ethanol, while ethyl alcohol contains about 5% water, often a disadvantage." Thus, Remington teaches away from using between about 0.2 and 13% by volume of a C1-C3 alcohol or C2-C4 diol. For the reasons stated above, it is asserted that a *prima facie* case of obviousness has not been made, and withdrawal of this rejection over claims 1 and 7-8, 15, and 24 is respectfully requested.

CONCLUSIONS

All of the remarks in the final Office Action have been addressed, claims 1-10, 12-18, and 20-26 are believed to be in condition for allowance, and such action is respectfully requested. The fee for filing a Petition for a three month time extension is included with this response. Should any additional fees be due, the Examiner is authorized to charge any fee deficiency associated with this response to Deposit Account No. 50-1123. The Examiner is asked to kindly contact the undersigned by telephone should any outstanding issues remain.

Respectfully submitted,

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